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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/561,015 | 02/17/2006 | Dan P. Felsenfeld | 02420/100M761-US1 | 9430 |

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| EXAMINER | |
|---|---|
| WANG, CHANG YU | |
| ART UNIT | PAPER NUMBER |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/561,015 | FELSENFELD ET AL. | |
| | Examiner | Art Unit | |
| | Chang-Yu Wang | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 8-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/16/05* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/15/06,10/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Application/Election/Restrictions*

1. Applicant's election with traverse of Group II (claims 5-7) in the reply filed on June 2, 2008 is acknowledged. The traversal is on the ground(s) that all claims relate to a corresponding special technical feature, the polypeptide of SEQ ID NO.2 and its use for promoting neurite outgrowth, and the technical feature of SEQ ID NO:2 is not known in the prior art because SEQ ID NO:2 is different from the known cytoplasmic domains of L1 protein, in particular tyrosine residue (Tyr) at the C-terminus of the protein is replaced by phenylalanine (Phe). Applicant's arguments have been fully considered but they are not found persuasive. Claim 1 directed to a method of promoting neurite outgrowth of a mammalian neuron (A) comprising inhibiting the binding of an ankyrin protein of the neuron to a L1-CAM protein by contacting the neuron with a peptide comprising SEQ ID NO:2. First, the method of promoting neurite outgrowth using L1-CAM is known as set forth in the previous office action (US6576607). Although US6576607 does not explicitly teach SEQ ID NO:2, an L1-CAM protein comprising SEQ ID NO:2 is also known in the art because the claimed peptide recites “comprising” SEQ ID NO:2. See Garver et al. (J. Cell Biol. 1997. 137: 703-714) on p. 705, 1$^{st}$ col., 4$^{th}$ paragraph or p. 708, 1$^{st}$ col., 2nd paragraph to 2$^{nd}$ col.1$^{st}$ paragraph or See Tuvia et al. (Proc. Natl. Acad. Sci. USA 1997. 94: 12957-129562) on p. 12960, 2nd col. Therefore, claim 1 does not recite a special technical feature defined by the PCT rules as a feature that defines a contribution over the prior art. Since the 1$^{st}$ claimed invention has no special technical feature, it cannot share a special technical feature with the other

claimed inventions. Thus, Applicant's inventions do not have a single inventive concept and so lack unity of invention.

In addition, the examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The requirement for the rest of restriction is still deemed proper and is therefore made FINAL.

2. Claims 1-17 are pending. Claims 1-4 and 8-17 are withdrawn with traverse from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 5-7 are under examination in this office action.

***Drawings***

3. The drawings/figures 7A, 7B, 8A and 8B are objected to because sequence listings included in the specification must not be duplicated in the drawings. See 37 C.F.R. §1.58(a) and §1.83. Appropriate correction is required.

***Specification***

4. The instant abstract is objected to because the abstract contains more than 150 words in length. Appropriate correction is required.

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The elected invention is directed to an isolated peptide for treating axonal damage, which is a product not a process. The title should be related to a product not a process.

### *Claim Objections*

5. Claim 5 is objected to because of the following informalities: the article “an” (i.e. an isolated) is missing before the limitation "peptide” as recited in the line 3 of the claim. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising an isolated peptide comprising or consisting of the amino acid sequence of SEQ ID NO:2 and a pharmaceutical acceptable carrier or enabling for a pharmaceutical composition comprising a fusion protein consisting of the amino acid sequence of SEQ ID NO:2

fused to the amino acid sequence of SEQ ID NO:6 and a pharmaceutical acceptable carrier for inhibiting binding of an ankyrin protein to L1-CAM and thereby to promote neurite outgrowth in neurons in vitro or in vivo, does not reasonably provide enablement for a pharmaceutical composition comprising the amino acid sequence of SEQ ID NO:2 and a pharmaceutical acceptable carrier for treating all forms of diseases characterized by axonal damage selected from spinal cord injury, traumatic brain injury, stroke and neurodegenerative diseases as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

"There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'. These factors include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)". See MPEP § 2164.01.

**Breadth of the claims**: Claim 5 is drawn to a pharmaceutical composition comprising the amino acid sequence of SEQ ID NO:2 and a pharmaceutical acceptable carrier for treating all forms of diseases characterized by axonal damage selected from spinal cord injury, traumatic brain injury, stroke and neurodegenerative diseases. The

instant claim encompasses a pharmaceutical composition comprising a peptide comprising the amino acid sequence of SEQ ID NO:2 for treatment of all forms of diseases caused by different mechanisms.

**Nature of the invention**: The instant invention is based on the finding that modulation of L1-CAM adhesion receptor-ankyrin cytoskeleton interactions plays an essential role in the regulation of neuronal outgrowth. The specification teaches that NGF stimulates phosphorylation of tyrosine residue of the L1-CAM cytoplasmic domain, and thereby inhibits ankyrin binding. The specification states that phenylalanine substitution for tyrosine 1229 of L1-CAM (L1-CAM-YF) induces constitutive ankyrin binding in other vertebrate L1 family members, and histidine substitution for tyrosine 1229 (L1-CAM-YH) inhibits ankyrin binding. The specification also shows that a peptide consisting of the amino acid sequence of SEQ ID NO:2 or a peptide consisting of the amino acid sequence SEQ ID NO:2 fused to the amino acid sequence SEQ ID NO:6 (AP-YF) enhances neurite outgrowth in cerebellar neuronal cultures. The specification also shows that AP-YF can inhibit Ankyrin binding to L1-CAM.

**State of the prior art/predictability/experimentation:** Although the specification shows that AP-YF, a peptide consisting of the amino acid sequence of SEQ ID NO:2 fused to the amino acid sequence of SEQ ID NO:6 can promote neurite outgrowth in vitro, neither the specification nor the prior art teaches that a pharmacological composition comprising such peptide can be used to treat all forms of diseases as recited in instant claim 5. Although the specification provides a prophetic example of use of the claimed peptide in an animal model of spinal cord injury, the

specification fails to show that the claimed peptide indeed is effective in treating such injury. Based on the specification and the prior art, Applicant is only enabled for promoting neurite outgrowth by the claimed pharmaceutical composition. However, the claims are not limited to neurite outgrowth as set forth above but also to the treatment of all possible diseases, which is not supported by the specification or the prior art.

The instant claim encompasses a pharmaceutical composition comprising a peptide comprising the amino acid sequence of SEQ ID NO:2 for treatment of all forms of diseases caused by different mechanisms. However, the specification fails to establish that all different diseases caused by different mechanisms can be treated with the same drugs or having the same effects with the same drugs. One treatment for one specific disorder does not apply to another disorder. It is well known in the art that neurodegenerative disorders characterized by lesions of the CNS, have different symptoms, pathologies, and etiologies and the treatment of these disorders is complex and problematic. For example, no treatment or administration was known to prevent or cure neurodegeneration or demyelination disorders caused by neurodegeneration, such as multiple sclerosis (MS), which is characterized as an autoimmune disorder mainly affecting young adults and characterized by destruction of myelin in the central nervous system and its pathologic findings include demyelination throughout the white matter of the central nervous system (see p. 375, first paragraph, 't Hart et al. Curr. Opin. Neurol. 2003. 16: 375-383). Parkinson's disease is characterized by defects in motor function, e.g. resting tremor, rigidity of extremities and neck, shortened steps with minimal arm swinging, and stooped posture, due to the progressive loss of dopaminergic neurons in

the substantia nigra pars compacta. Amyotrophic lateral sclerosis is characterized by the slow but inevitable degeneration of α motor neurons in the spinal cord ventral horns and brainstem and neurons in the motor cortex leading to eventual paralysis and death. Alzheimer's disease involves an initial loss of recent memory function and attention, followed by failure of language skills, visual-spatial orientation, abstract thinking, and judgment and alterations of personality. The histopathology involves collections of neurofibrillary tangles and senile plaques and diffuse loss of neurons. Since there is no established correlation among these different forms of lesions or damage or degeneration, it is unpredictable whether a treatment for one type of injury or lesion could be applied to other types of diseases or lesions.

It is also known in the art that the regeneration in the central nervous system is still a challenge. Several molecules have been identified to inhibit remyelination in the CNS and axonal/neurite regeneration, myelin-associated molecules such as Nogo, MAG, and proteoglycans in the extracellular matrix, (see Schmidt et al. Annu. Rev. Biomed. Eng. 2003. 5: 293-347 and p. 450, 2nd col. Hoke et al. Nat. Clin. Pract. Neurol. 2006: 448-454). The nerve injury of the CNS in vivo results in generation of glial scars, which inhibits nerve regeneration of the CNS (Hoke et al. Nat. Clin. Pract. Neurol. 2006: 448-454). Neither the specification nor the prior art teaches that degeneration of the CNS in vivo can be regenerated by any given agent.

While the skill level in the art is high, the level of predictability is low. Given the highly unpredictable nature of treating any CNS lesion in any patient, one of skill in the art could not be reasonably assured that the disclosed invention would be effective for

the treatments of different diseases.

Thus, in view of the breadth of the claims, the complex nature of the invention, the limited working examples, the necessity of experimentation, the unpredictability of the art, and the lack of sufficient guidance in the specification, undue experimentation would be required of the skilled artisan to practice the claimed invention as it pertains to the claimed pharmaceutical composition for treatment of all forms of diseases.

### *Claim Rejections - 35 USC § 102*

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by either Tuvia et al. (Proc. Natl. Acad. Sci. USA. 1997. 94: 12957-129562, as in IDS) as evidenced by Davis et al. (J. Cell Biol. 1996, 135:1355-1367).

Claims 5-6 are drawn to a peptide comprising an amino acid sequence consisting of SEQ ID NO:2 and a pharmaceutical composition comprising the amino acid sequence of SEQ ID NO:2 and a pharmaceutical acceptable carrier for treating diseases characterized by axonal damage selected from spinal cord injury, traumatic brain injury, stroke and neurodegenerative diseases.

Tuvia et al. teach a peptide comprising the amino acid sequence of instant SEQ ID NO:2, which meets the limitation as recited in instant claims 5-6 because of the

recitation “comprising” (see p. 12960, 2nd col.). Although Tuvia et al. do not explicitly teach SEQ ID NO:2, Tuvia et al. teach a protein of neurofascin (or L1) with a mutation of tyrosine in the motif of “FIGQY” substituted by phenylalanine (F). The amino acid sequence of neurofascin meets the limitation of “a peptide comprising SEQ ID NO:2” as evidenced by Davis et al. (see the sequence alignment below and see p. 1362, figure 7). In addition, Tuvia et al. also teach a composition comprising neurofascin with a motif of “FIGQF" in an immunoprecipitation buffer (see p. 12959, cols 1-2), which also meets the limitation of “a pharmaceutically acceptable carrier” as recited in instant claim 5. Furthermore, the intended use for treating different diseases as recited in instant claim 5 is not given patentable weight because the structure and composition of the claimed invention is identical to the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Therefore, claims 5 and 6 are anticipated by Tuvia et al.

The sequence search results disclose as follows:

```
Q9QVN5_9MURI
ID   Q9QVN5_9MURI            Unreviewed;      1151 AA.
AC   Q9QVN5;
DT   01-MAY-2000, integrated into UniProtKB/TrEMBL.
DT   01-MAY-2000, sequence version 1.
DT   24-JUL-2007, entry version 36.
DE   NEUROFASCIN isoform.
OS   Rattus sp.
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi;
OC   Muroidea; Muridae; Murinae; Rattus; unclassified Rattus.
OX   NCBI_TaxID=10118;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RX   MEDLINE=97103184; PubMed=8947556; DOI=10.1083/jcb.135.5.1355;
RA   Davis J.Q., Lambert S., Bennett V.;
RT   "Molecular composition of the node of Ranvier: identification of
RT   ankyrin-binding cell adhesion molecules neurofascin (mucin+/third
RT   FNIII domain-) and NrCAM at nodal axon segments.";
RL   J. Cell Biol. 135:1355-1367(1996).
CC   ---------------------------------------------------------------------
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---------------------------------------------------------------------
DR   HSSP; Q92823; 1UEY.
DR   GO; GO:0005515; F:protein binding; IEA:UniProtKB-KW.
DR   GO; GO:0007155; P:cell adhesion; IEA:UniProtKB-KW.
DR   InterPro; IPR003961; FN_III.
DR   InterPro; IPR008957; FN_III-like.
DR   InterPro; IPR013151; Ig.
DR   InterPro; IPR007110; Ig-like.
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DR   InterPro; IPR013783; Ig-like_fold.
DR   InterPro; IPR013098; Ig_I-set.
DR   InterPro; IPR003599; Ig_sub.
DR   InterPro; IPR003598; Ig_sub2.
DR   Gene3D; G3DSA:2.60.40.30; FN_III-like; 3.
DR   Gene3D; G3DSA:2.60.40.10; Ig-like_fold; 5.
DR   Pfam; PF00041; fn3; 4.
DR   Pfam; PF07679; I-set; 5.
DR   Pfam; PF00047; ig; 1.
DR   SMART; SM00060; FN3; 4.
DR   SMART; SM00409; IG; 2.
DR   SMART; SM00408; IGc2; 4.
DR   PROSITE; PS50853; FN3; 4.
DR   PROSITE; PS50835; IG_LIKE; 6.
PE   4: Predicted;
KW   Immunoglobulin domain; Repeat.
SQ   SEQUENCE   1151 AA;  129733 MW;  770BD492C4A4ECC5 CRC64;

  Query Match             95.4%;  Score 62;  DB 2;  Length 1151;
  Best Local Similarity   91.7%;  Pred. No. 0.054;
  Matches   11;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 QFNEDGSFIGQF 12
              |||||||||||:
Db       1112 QFNEDGSFIGQY 1123
```

8. Claims 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Garver et al. (J. Cell Biol. 1997. 137: 703-714, as in IDS) as evidenced by Davis et al. (J. Cell Biol. 1996, 135:1355-1367).

Claims 5-6 are drawn to a peptide comprising an amino acid sequence consisting of SEQ ID NO:2 and a pharmaceutical composition comprising the amino acid sequence of SEQ ID NO:2 and a pharmaceutical acceptable carrier for treating diseases characterized by axonal damage selected from spinal cord injury, traumatic brain injury, stroke and neurodegenerative diseases.

Garver et al. teach a peptide comprising the amino acid sequence of instant SEQ ID NO:2, which meets the limitation as recited in instant claims 5-6 because of the recitation “comprising” (on p. 705, 1st col., 4th paragraph or p. 708, 1st col., 2nd paragraph to 2nd col.1st paragraph.). Although Garver et al. do not explicitly teach SEQ ID NO:2, Garver et al. teach a protein of neurofascin (or L1) with a mutation of tyrosine in the motif of “FIGQY” substituted by phenylalanine (F). The amino acid sequence of

neurofascin meets the limitation of "a peptide comprising SEQ ID NO:2" as evidenced by Davis et al. (see the sequence alignment above and see p. 1362, figure 7). In addition, Garver et al. also teach a composition comprising neurofascin with a motif of "FIGQF" in an immunoprecipitation buffer or a buffer for ankyrin binding assay (see p. 708-709, figure 4), which also meets the limitation of "a pharmaceutically acceptable carrier" as recited in instant claim 5. Furthermore, the intended use for treating different diseases as recited in instant claim 5 is not given patentable weight because the structure and composition of the claimed invention is identical to the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Therefore, claims 5 and 6 are anticipated by Garver et al.

### *Claim Rejections - 35 USC § 103*

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tuvia et al. (Proc. Natl. Acad. Sci. USA. 1997. 94: 12957-129562, as in IDS) or Garver et al. (J. Cell Biol. 1997. 137: 703-714, as in IDS) as evidenced by Davis et al. (J. Cell Biol. 1996, 135:1355-1367)in view of US 6025140 (Langel et al. issued Feb 15, 2000).

Claims 5-6 are drawn to a peptide comprising an amino acid sequence consisting of SEQ ID NO:2 and a pharmaceutical composition comprising the amino acid sequence of SEQ ID NO:2 and a pharmaceutical acceptable carrier for treating diseases characterized by axonal damage selected from spinal cord injury, traumatic brain injury, stroke and neurodegenerative diseases. Claim 7 is drawn to a peptide comprising an amino acid sequence consisting of SEQ ID NO:2 linked to an isolated peptide comprising an amino acid sequence of SEQ ID NO:6.

Tuvia et al. and Garver et al. are as set forth above but fail to teach the amino acid sequence of SEQ ID NO:6 that is fused to the peptide comprising SEQ ID NO:2 as recited in instant claim 7.

US 6025140 (the'140 patent) teaches that peptides containing the antennapedia homeodomain pAntp (43-58) (SEQ ID NO:4) enhance their penetration into the cell membrane and can be effectively internalized by the cells (see col. 14, line 56-col.15, line2). The amino acid sequence of SEQ ID NO:4 of the '140 patent has an amino acid sequence 100% identical to the amino acid sequence of SEQ ID NO:6 (see the sequence alignment below).

It would have been obvious to a skilled artisan at the time the instant invention was made to fuse the peptide comprising SEQ ID NO:2 to an peptide comprising SEQ ID NO:6 to enhance the membrane penetration of the claimed peptide into the cell. The person of ordinary skill in the art would have been motivated to do so with an expectation of success because the antennapedia homeodomain comprising SEQ ID NO:6 has been successfully used to enhance peptide-penetration into the cell.

The sequence search results disclose as follows:

```
US-09-116-294-4
; Sequence 4, Application US/09116294
; Patent No. 6025140
; GENERAL INFORMATION:
;  APPLICANT: Langel, Ulo
;  APPLICANT: Bartfai, Tamas
;  APPLICANT: Pooga, Margus
;  APPLICANT: Valkna, Andres
;  APPLICANT: Saar, Kulliki
;  APPLICANT: Hallbrink, Mattias
;  TITLE OF INVENTION: Conjugated Constructs of Peptides and
;  TITLE OF INVENTION: Nucleic Acid Analogs, and Their Transport Across Membranes
;  FILE REFERENCE: 4394
;  CURRENT APPLICATION NUMBER: US/09/116,294
;  CURRENT FILING DATE: 1998-07-16
;  EARLIER APPLICATION NUMBER: 60/052,678
;  EARLIER FILING DATE: 1997-07-24
;  NUMBER OF SEQ ID NOS: 16
;  SOFTWARE: FastSEQ for Windows Version 3.0
; SEQ ID NO 4
;   LENGTH: 16
;   TYPE: PRT
;   ORGANISM: drosphila
US-09-116-294-4

  Query Match             100.0%;  Score 16;  DB 2;  Length 16;
  Best Local Similarity   100.0%;  Pred. No. 2.4e-10;
  Matches   16;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 RQIKIWFQNRRMKWKK 16
              ||||||||||||||||
Db          1 RQIKIWFQNRRMKWKK 16
```

## *Conclusion*

10. NO CLAIM IS ALLOWED.

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
August 18, 2008

/Christine J Saoud/
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